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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/376,604	08/18/1999	RAGUPATHY MADIYALAKAN	AREX-P03-004	6693

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EXAMINER	
NICKOL, GARY B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/376,604	MADIYALAKAN ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *243,244 and 247-250* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 113,117-120,123,125,129-135,137-139,141-144,170-175,180-182,185,187,190-204,206-209 and 235-257.

Continuation of Disposition of Claims: Claims rejected are 113,117-120,123,125,129-135,137-139,141-144,170-175,180-182,185,187,190-204,206-209,235-242,245,246 and 251-257.

Response to Amendment

The Amendment filed December 29, 2003 in response to the Office Action of September 25, 2003 is acknowledged and has been entered.

Claims 113, 117-120, 123, 125, 129-135, 137-139, 141-144, 170-175, 180-182, 185, 187, 190-204, 206-209, and 235-257 are pending.

Claims **243-244, 247-250** have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 113, 117-120, 123, 125, 129-135, 137-139, 141-144, 170-175, 180-182, 185, 187, 190-204, 206-209, and 235-242, 245-246, 251-257 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Election/Restrictions

Newly submitted claims 243-244 and 247-250 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 243-244 define the antigen as a *cell-surface-associated antigen with a carbohydrate moiety* which is independent and or distinct from the originally examined invention drawn to a multi-epitopic antigen present in a host's serum. Further, the originally elected invention (Group I, restriction mailed 02-09-01) did not include claims with the limitation of a cell-surface-

associated antigen with a carbohydrate moiety and would have been restricted from the invention claimed in Group I.

Claims 247-250 are further directed to an invention that is independent or distinct from the invention originally claimed. Claims 247-250 are drawn to "photoactivated" binding agents. Since the photoactivation of such agents includes exposing the binding agents to radiation, (see specification, page 37), the claims no longer read on the elected invention, drawn to non-radiolabeled binding agents.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 243-244 and 247-250 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Rejections Maintained:

Claims 113, 117-120, 123, 131-135, 137-139, 141-144, 170-175, 180-182, 185, 190, 193-204, 206-209, 235-239 remain rejected and new claims 240-242, 245-246, and 251-253 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 5,532,159 (Webb *et al.* April 1, 1994) for the reasons of record in the Action mailed September 25, 2003.

Applicants argue (last paragraph, page 13) that the patented reference differs from the claims in that the reference teaches that it is believed that OFP is immunosuppressive and by sequestering or removing OFP via the monoclonal antibody, the patient's immune defense is released from impairment allowing a more efficient and natural rejection of the cancer. Applicants assert (page 14) that this is a significant difference from the claimed invention

because anti-OFP antibodies "work" because they sequester or remove OFP from circulation such that is no longer available to the immune system. Applicants add that if the complex (anti-OFP antibody + OFP) is unavailable, an effective immune response against a second previously un-exposed epitope of OFP cannot be generated. Thus, applicants essentially argue that the claimed functional limitations are not an inherent property of the referenced method. This argument has been considered but is not found persuasive.

The suggestion that anti-OFP antibodies achieve anti-tumor activity *in vivo* by releasing an innate immunosuppressive mechanism is, at best, speculative. In other words, the inventors' ('159 inventors) "belief" does not remove the possibility that other mechanisms are responsible for the observed anti-tumor effects of the anti-OFP antibodies. Further, the suggestion that an effective immune response against a second previously un-exposed epitope of OFP would *not* be generated is ill founded. Applicants appear to be defining the complexity of the immunological response into discrete steps: (1) *in vivo* binding of anti-OFP antibodies to OFP, (2) removal of OFP. However, the immune response is not so predictable and discrete. There are hundreds of possible biological processes, events, and mediators that may account for an observed humoral and or cell-mediated response. Thus, even if the anti-OFP/OFP complex is removed, its removal does not eliminate the possibility that a different or second OFP epitope was exposed to the immune system, thus facilitating an anti-tumor response. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Claims 113, 117-120, 123, 125, 129-135, 137-139, 141-144, 170-175, 180-182, 185, 187, 190-204, 206-209, 235-239 remain rejected and new claims 240-242, 245-246, 251-257 are

rejected under 35 U.S.C. 103(a) as being unpatentable over Baum *et al.* (Hybridoma, Vol. 12, No. 5, 1993, pages 583-589) **or** Madiyalakan *et al.* (Hybridoma, Volume 14, No. 2, May 19, 1995) in further view of US Patent No. 5,532,159 (Webb *et al.* April 1, 1994) for the reasons of record in the Action mailed September 25, 2003.

Applicants argue that the teachings of Baum *et al.* and Madiyalakan *et al.* do not provide any motivation to make non-radiolabeled antibody or fragment as recited in the instant claims as a therapeutic agent because the references themselves teach administration of radiolabeled antibodies. This argument has been considered but is not found persuasive. The motivation to use non-radiolabeled antibodies was clearly set forth in the prior action based on the successful teachings of Webb *et al.* ('159). Recall, that Webb *et al.* also cautioned against the use of conjugating antibodies to radioisotopes because of toxic side effects and that their invention provides a low-cost, less toxic anti-cancer immunotherapy which enhanced the host's immune system's ability to destroy or contain cancers (Webb *et al.*, column 2, lines 10 and 40).

Applicants further add that the deficiencies of the '159 patent, having been discussed *supra*, cannot cure the deficiencies of Baum *et al.* or Madiyalakan *et al.* This argument has been considered but is not found persuasive because the 102 rejection above has been maintained.

Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Additionally, the specification remains objected to and claims drawn to specific biological deposits (i.e. Claims 125, 187) remain rejected under 35 USC 112, 1st paragraph for the reasons for record. Although applicants state for the record (page 12) that the mouse

hybridoma B43.13, which makes the antibody A1t-2, was deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, on May 18, 2000, and was given ATCC deposit number PTA-1883, the statement does not remedy the rejection of record. Applicants have not stated that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

New Objections/Rejections:

Claim Objections

Claims 125 and 187 objected to for reciting "produceable", which is spelled incorrectly.

Claim 240 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 142.

Claim 245 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 143.

Claim 246 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 144.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper to object to the claims as being substantial duplicates. See MPEP § 706.03(k).

Claims 190, and 238 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of an antibody which is "non-human" (Claim 190) has no clear support in the specification and the claims as

originally filed. Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection/objection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN
March 10, 2004

GARY NICKOL
PRIMARY EXAMINER